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EXAMINER	
KERR, KATHLEEN M	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 03/10/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/941,936	BATHE ET AL.	
	Examiner	Art Unit	
	Kathleen M Kerr	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 December 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *14,16-18,21 and 25-29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *14,16-18,21 and 25-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Application Status

1. In response to the previous Office action, a non-final rejection (mailed on August 23, 2003), Applicants filed a response and amendment received on December 23, 2003. Said amendment cancelled Claims 15, 19, 20, and 22-24 and amended Claims 14, 16-18, and 25-29. Thus, Claims 14, 16-18, 21, and 25-29 are pending in the instant Office action and will be examined herein.

Priority

2. As previously noted, the instant application is granted the benefit of priority for the foreign application 10043332.4 filed in Germany on September 2, 2000 and application 10033426.5 filed in Germany on July 10, 2001. Translations of said documents have been received on December 23, 2003.

Withdrawn - Objections to the Specification

3. Previous objection to the specification because the title is not descriptive is withdrawn by virtue of Applicants' amendment.

Maintained - Objections to the Specification

4. Previous objection to the Abstract for not completely describing the disclosed subject matter is maintained. Applicants' amendment to the Abstract is insufficient to address the objection previously presented. As previously noted, "in many databases and in foreign countries, the Abstract is crucial in defining the disclosed subject matter, thus, its completeness

is essential. The Examiner suggests the inclusion of the source species [of the sigC gene], *Corynebacterium glutamicum* for completeness." Clarification and/or amendment are required.

Withdrawn - Objections to the Claims

5. Previous objection to Claims 22 and 23 under 37 C.F.R. § 1.75 as being duplicate claims is withdrawn by virtue of Applicants' cancellation of said claims.

6. Previous objection to Claim 27 under 37 C.F.R. § 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim is withdrawn by virtue of Applicants' amendment to further limit coryneform in Claim 14 to *Corynebacterium glutamicum* in Claim 27.

Withdrawn - Claim Rejections - 35 U.S.C. § 112

7. Previous rejection of Claims 15-16 under 35 U.S.C. § 112, second paragraph, as being indefinite is withdrawn by virtue of Applicants' amendment canceling Claim 15 and making the step of isolation in Claim 16 clear.

8. Previous rejection of Claims 19-20 under 35 U.S.C. § 112, second paragraph, as being indefinite for the metes and bounds of the cited "pathways" is withdrawn b virtue of Applicants' cancellation of said claims.

9. Previous rejection of Claims 22-23 under 35 U.S.C. § 112, second paragraph, as being indefinite for the phrase "expression ... is enhanced" is withdrawn by virtue of Applicants' cancellation of said claims.

10. Previous rejection of Claim 24 under 35 U.S.C. § 112, second paragraph, as being indefinite for the term "regulatory properties" of the sigC polypeptide is withdrawn by virtue of Applicants' cancellation of said claims.

11. Previous rejection of Claims 25-26 under 35 U.S.C. § 112, second paragraph, as being indefinite for, the listed genes is withdrawn by virtue of Applicant's amendment.

12. Previous rejection of Claim 25 under 35 U.S.C. § 112, second paragraph, as being indefinite for the phrase "the gene lysE coding for lysine export" is withdrawn by virtue of Applicant's amendment

13. Previous rejection of Claims 14-27 and 29 under 35 U.S.C. § 112, first paragraph, written description, is withdrawn by virtue of Applicants' amendment requiring an exact structural limitation on the sigC gene.

14. Previous rejection of Claim 24 under 35 U.S.C. § 112, first paragraph, enablement, as failing to comply with the enablement requirement, is withdrawn by virtue of Applicants' cancellation of said claim.

15. Previous rejection of Claims 14-17, 19-22, and 24-29 under 35 U.S.C. § 112, first paragraph, scope of enablement, because the specification, while being enabling for methods using coryneform bacteria with overexpressed sigC and/or amino acid biosynthetic genes and with deleted amino acid reduction genes, does not reasonably provide enablement for methods using bacteria with enhancement and/or switching off or attenuation of such genes is withdrawn by virtue of Applicants' amendment. This rejection is reiterated below under new issues.

Maintained - Claim Rejections - 35 U.S.C. § 112

16. Previous rejection of Claims 14, 16-18, 21, and 25-29 under 35 U.S.C. § 112, second paragraph, is maintained. Applicants' arguments have been fully considered but are not deemed persuasive. Applicants argue that the amendment to the claims has obviated the rejection; the Examiner disagrees. While it is clear what an RNA polymerase sigma factor is (see molecular biology textbooks), the activity intended is wholly unclear. Is the activity to induce antibodies to the sigC protein? To help an RNA polymerase function? To help recognize a particular consensus sequence of DNA? Clarification is required.

The Examiner notes that because the nucleotide sequence overexpressed in the methods is exactly SEQ ID NO:1, no functional language is required in the claim. Thus, to obviate the instant rejection, the Examiner suggests simply deleting the "activity" phrase all together.

17. Previous rejection of Claim 25 under 35 U.S.C. § 112, first paragraph, scope of enablement, because the specification, while being enabling for methods using known feedback-resistance aspartate kinase and threonine dehydratase, does not reasonably provide enablement for methods using unknown feedback-resistance aspartate kinase and threonine dehydratase, is maintained. Applicants have not addressed this issue. Since the instant Office action is non-final, Applicants are invited to address this issue in response to the instant Office action.

To reiterate the previous rejection:

"The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Identifying novel feedback-resistance aspartate kinase and/or threonine dehydratase polypeptides for use in the claimed methods would require undue experimentation. The factors to be considered in determining whether undue experimentation is required are summarized above.

The specification provides a single example of each of the named polypeptides but provides no guidance for the identification of new ones. The state of the art is such that a finite number of feedback-resistant aspartate kinases and threonine dehydratases are known; these are enabled. However, the predictability of finding other feedback-resistant aspartate kinases and threonine dehydratases is minute. Thus, the instant claim is not enabled to the full extent of its scope."

18. Previous rejection of Claims 28-29 under 35 U.S.C. § 112, first paragraph, enabling deposit, is maintained. Applicants have not addressed this issue. Since the instant Office action is non-final, Applicants are invited to address this issue in response to the instant Office action.

As previously noted, "To practice the instant methods, one of skill in the art is required to use DH5αmcr/pEC-XK99EsigCb2ex or DSM5715/pEC-XK99E. While the instant specification contains limited deposit information on page 19, the requirements to enable such a deposit have not been fully met by the instant application. To enable the instant claims by enabling the deposit of DSM 12968, the following items are required: (1) the accession number assigned by the depository, (2) the date of deposit, (3) a brief description of the deposit, (4) the name and **full address** of the depository (37 C.F.R. § 1.801 - 1.809) (those which are in bold have not been fulfilled by the instant specification), **and (5)** the record must also contain a statement certifying that all restrictions on accessibility to said deposit be irrevocably removed by Applicant upon the

granting of the patent (see M.P.E.P. § 2404.01); this statement may be certified by Applicants or Applicants' representative."

Withdrawn - Claim Rejections - 35 U.S.C. § 102

19. Previous rejection of Claims 14-18, 21-23, and 27 under 35 U.S.C. § 102(b) as being anticipated by Kimura *et al.* (EP 0864654) is withdrawn by virtue of Applicants' amendment clarifying the identify of the sigma C factor overexpressed in the claimed methods.

20. Previous rejection of Claims 14-18, 21-23, and 27 under 35 U.S.C. § 102(a)[previously incorrectly noted as a (b) type rejection] as being anticipated by Nakagawa *et al.* (EP 1108790) is withdrawn by virtue of Applicants' filing of a translation of the foreign priority document DE 10043332.4, which document has support for the claimed invention as of September 2, 2000, which does not pre-date Nakagawa *et al.*

NEW ISSUES

Claim Rejections - 35 U.S.C. § 112

The following is a quotation of the second paragraph of 35 U.S.C. § 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

21. Claims 25 and 26 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In these claims, various additional genes are noted. The inclusion of both the gene name (or abbreviation) and the enzyme name is confusing. For

example, if a gene for glucose-6-phosphate dehydrogenase was named gpd and not "zwf" as required in the claims, would this read on the claim or not? Many genes are incorrectly identified during genome projects and the like, thus using gene names to identify any gene encoding a particular enzyme is confusing. The Examiner suggests removal of the gene name limitation entirely.

Also in Claims 25 and 26, the nature of the following proteins is unclear: "a protein for lysine export", "a Zwa1 protein", and "a Zwa2 protein". These proteins are unclear as to their metes and bounds from simply their name or their function. While the specification gives references for specific examples of these proteins, no limitation to these specific proteins can be read into the claims. Thus, one of skill in the art would unclear as to the genus of genes encoding a protein for lysine export, for example. Clarification is required.

22. Claim 28 is rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The use of a strain of DH5α that is a Corynebacterium glutamicum is wholly confusing because DH5α is an *E. coli* strain (see page 19 of the instant specification, for example). Clarification is required.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

23. Claim 25 is rejected under 35 U.S.C. § 112, first paragraph, written description, as containing subject matter which was not described in the specification in such a way as to

reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claim 25 is drawn to a method optionally using genes for feedback-resistant aspartate kinase and feedback-resistant threonine dehydratase wherein said gene is claimed solely by function and without any structural limitations.

The Court of Appeals for the Federal Circuit has recently held that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as be structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." University of California v. Eli Lilly and Co., 1997 U.S. App. LEXIS 18221, at *23, quoting Fiers v. Revel, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original). To fully describe a genus of genetic material, which is a chemical compound, applicants must (1) fully describe at least one species of the claimed genus sufficient to represent said genus whereby a skilled artisan, in view of the prior art, could predict the structure of other species encompassed by the claimed genus and (2) identify the common characteristics of the claimed molecules, e.g., structure, physical and/or chemical characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or a combination of these.

In the instant specification, a single example of both feedback-resistant enzymes is described in the specification. No description of what makes these enzymes feedback-resistant is described. Thus, one of skill in the art would be unable to predict the structure of other genes encoding these feedback resistant enzymes. Therefore, claims drawn to methods using said genes are not adequately described.

24. Claims 25-26 are rejected under 35 U.S.C. § 112, first paragraph, written description, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claims 25-26 are drawn to a method optionally using genes for proteins by name only wherein said gene is claimed solely by function and without any structural limitations.

The Court of Appeals for the Federal Circuit has recently held as described above. While genes encoding known enzymes with particular functions, such as genes encoding dihydrodipicolinate synthase, are adequately described by virtue of their specification function and their examples in the art, this is not the case for genes encoding proteins without clear support in the art for their genus: a protein for lysine export, Zwa1 protein, and Zwa2 protein. The mere name of these proteins does NOT connote a structure and/or function as is the case with the specific enzymes noted elsewhere in the claims. One example of each is noted in the specification; however, no description of how to maintain Zwa1-like protein structure and/or function is found. Thus, one of skill in the art would be unable to predict the structure of other members of the genus of genes claimed.

25. Claims 14, 16-18, 21, and 25-29 are rejected under 35 U.S.C. § 112, first paragraph, scope of enablement, because the specification, while being enabling for overexpressing SEQ ID NO:1 by transforming a host cell with a vector comprising SEQ ID NO:1 and a promoter, does not reasonably provide enablement for overexpressing SEQ ID NO:1 by means otherwise mentioned in the specification. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate

in scope with these claims. To practice the claimed invention to the full extent of its scope would require undue experimentation.

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The Court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. While all of these factors are considered, a sufficient amount for a *prima facie* case is discussed below.

In the specification on page 12 (paragraph [0038]), means of overexpression are described. Said means include not only increasing the copy number of a gene or regulating the gene with a particular promoter, which means are enabled by the art, but also include altering the ribosome binding site, altering the lifetime of the mRNA, altering the protein so as to prevent degradation, and altering media conditions, all of which are known in the art to "overexpress" a

gene in specific examples, but none of which are predictable with sigC or other genes that lack specific examples in the art. The specification provides no working examples or direction for overexpression using means of ribosome binding site, altering the lifetime of the mRNA, altering the protein so as to prevent degradation, and altering media conditions. The nature of the invention is that these means are specific to a particular gene sequence and cannot be extrapolated from other, unrelated genes; there is no particular recipe of media that will overexpress all genes. Thus, overexpression using these methods is wholly unpredictable and not enabled by the specification or the art.

Claims 21, 28 and 29 are included in the instant rejection because the use of the vector does not limit the concept of "overexpression" in Claim 14.

26. Claims 25-26 are rejected under 35 U.S.C. § 112, first paragraph, scope of enablement, because the specification, while being enabling for methods using known zwa1, zwa2, and lysC genes as described in the specification, does not reasonably provide enablement for methods using other of these genes. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims. To practice the claimed invention to the full extent of its scope would require undue experimentation.

The factors to be considered in determining whether undue experimentation is required are summarized.

The instant specification teaches particular examples of lysC, zwa1, and zwa2 from the art. The art fully enables using these particular genes. While the instant specification describes and enables means for identifying other lysC, zwa1, and zwa2 genes using hybridization

methods, etc., these methods do not enable one of skill in the art to make all, or a relevant portion of, the polynucleotides within the scope of the claims because the ability to find a lysC, zwa1, and zwa2 gene, which is structurally related said sequences, is not equivalent to the ability to make a lysC, zwa1, and zwa2 genes as required by the statute (i.e., "make and use"). No description in the specification or the art provides particular residues whose encoding is important within the disclosed sequence so that its lysC-, zwa1-, and zwa2-nature is maintained. Thus, one of skill in the art would be unable to predict the structure of the other members of the genus in order to make such members. Therefore, the instant claims are not enabled to the full extent of their scope.

Summary of Issues

27. The following is a summary of the issues remaining in the instant application:

a) The Abstract stands objected to for not completely describing the disclosed subject matter.
b) Claims 14, 16-18, 21, and 25-29 stand rejected under 35 U.S.C. § 112, second paragraph, for the clarity of sigma C factor activity.
c) Claims 25 and 26 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for the nature of the various additional genes used.
d) Claim 28 stands rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for use of *E. coli* strain of DH5α.
e) Claim 25 stands rejected under 35 U.S.C. § 112, first paragraph, written description, for feedback-resistance aspartate kinase and threonine dehydratase.
f) Claims 25-26 stand rejected under 35 U.S.C. § 112, first paragraph, written description, for using various genes limited only by name.
g) Claims 14, 16-18, 21, and 25-29 stand rejected under 35 U.S.C. § 112, first paragraph, scope of enablement, for overexpression of SEQ ID NO:1 as based on the definition of overexpression in the specification.
h) Claim 25 stands rejected under 35 U.S.C. § 112, first paragraph, scope of enablement, for using unknown feedback-resistance aspartate kinase and threonine dehydratase.
i) Claims 25-26 stand rejected under 35 U.S.C. § 112, first paragraph, scope of enablement, because the specification, while being enabling for methods using known zwa1, zwa2, and lysC genes as described in the specification, does not reasonably provide enablement for methods using other of these genes.
j) Claims 28-29 stand rejected under 35 U.S.C. § 112, first paragraph, enabling deposit.

Conclusion

28. Claims 14, 16-18, 21, and 25-29 are not allowed for the reasons identified in the numbered sections of this Office action. Applicants must respond to the objections/rejections in each of the numbered sections in this Office action to be fully responsive in prosecution.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kathleen M Kerr whose telephone number is (571) 272-0931. The examiner can normally be reached on Monday through Friday, from 9:00am to 6pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathupura Achutamurthy can be reached on (571) 272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Kathleen M Kerr
Examiner
Art Unit 1652

March 5, 2004